

CONTINUOUS PATHS FOR THE ALLOSTERIC TRANSITIONS OF ISOLATED  $\alpha$ -  
AND  $\beta$ -SUBUNITS OF HEMOGLOBIN

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The allosteric mechanism of hemoglobin involves a substantial conformational change in which one  $\alpha\beta$  dimer in the tetramer rotates approximately  $15^\circ$  relative to the other  $\alpha\beta$  dimer. The tetrameric nature of the molecule is required for this transition, but it also demands changes in the conformations of the individual subunits. This paper reports continuous paths for the structural changes in the isolated subunits. While this is a theoretical situation, the comparison between these paths and one calculated for the entire tetramer (K. W. Olsen, S. Fischer & M. Karplus, Biophys. J. (2000) **78**:394A) should demonstrate the influence of quaternary structure on the allosteric mechanism. We have applied the Conjugate Peak Refinement method (S. Fischer & M. Karplus, Chem. Phys. Lett. (1992) **194**:252) to calculate the transitions between the T- and R- state subunit conformations. The simulations provide continuous, energetically plausible paths for both the  $\alpha$ - and the  $\beta$ - chains. Both isolated subunits can accomplish approximately 50% of their conformational change before the first saddle point on the path, which is significantly different than the path for the entire tetramer. The implications of these paths to the mechanism of the allosteric quaternary changes in the tetramer will be discussed.